REMARKS

The Office Action dated October 11, 2006 has been received and carefully studied.

The Examiner objects to claims 5-7 under 37 C.F.R. §1.75(c) as being improper multiple dependent claims. By the accompanying amendment, this informality has been addressed.

The Examiner rejects claims 1 and 3-8 under 35 U.S.C. §102(b) as being anticipated by Yokoyama et al., U.S. Patent No. 6,080,396, and as being anticipated by Sakurai, EP 0 397 307. The Examiner states that Yokoyama teaches a pharmaceutical preparation and the method to prepare it containing a copolymer of PEG and a polyamino acid which can include aspartic or glutameric acid as its monomer, the amino acid having a side chain carboxyl group that can be attached to an anthracycline-based anticancer agent. The Examiner adds that the process for producing the composition includes dissolving the block copolymer in solvents such as water or water mixed with a low-boiling organic solvent along with the drug, followed by concentration and freeze drying. The Examiner states that Sakurai teaches a water soluble block copolymer and the method of its production, wherein the copolymer contains a hydrophobic agent that can contain PEG and a hydrophobic section that can contain polyaspartic acid and polyglutamic acid, the amino acid having a side chain carboxyl group that can be attached to an anthracycline-based anticancer agent including adriamycin, e.g. doxorubicin. The Examiner adds that the process for producing the composition includes dissolving the block copolymer, adding

the drug dissolved in DMF, then adding EDC and stirring the solution for 19 hours.

By the accompanying amendment, the limitations of claim 2 have been incorporated into claims 1 and 8. In addition, claims 1 and 8 have been amended by deleting water as the solvent in which the block copolymer and drug are dissolved. It is believed that the amendment overcomes the rejection.

The Examiner also rejects claims 1-8 under 35 U.S.C. §103(a) as being unpatentable over Yokoyama et al., as being unpatentable over Yokoyama in view of Matsumara and in view of JP-A-2001-226294, and as being unpatentable over Sakurai et al. in view of Matsumara and in view of JP-A-2001-226294. The Examiner considers that it would have been obvious to use techniques other than dialysis and filtration for forming the drug, because Yokoyama discloses that replacing the solvent of the mixture solution with water by means of dialysis, ultrafiltration or the like shows that there are more ways to remove water. The Examiner also notes that the solvent can be water, and thus neither dialysis nor ultrafiltration would be necessary. The Examiner cites Matsumara for its disclosure that the use of dialysis or ultrafiltration on pharmaceuticals with contained drugs causes part of the drug to be removed, thereby suggesting use of another technique. JP '294 is cited for its disclosure of producing a macromolecular block copolymer-drug composite by steps other than dialysis or ultrafiltration.

By the accompanying amendment, water alone as the solvent has been removed from the claims.

The present invention relates to a process for manufacturing a micelle formed by a block copolymer, comprising the steps of dissolving a block copolymer composed of a hydrophilic polymer structure moiety and a hydrophobic polyamino acid structure moiety and drug in a mixed solvent of water and a low-boiling point organic solvent miscible with water, and distilling off the low-boiling point organic solvent. The micelle has a structure wherein the hydrophilic structure moiety is present outside, the hydrophobic polyamino acid structure moiety is present as the inner core, and the drug is capsulated therein. If the drug is not capsulated in the inner core of the micelle, the block copolymer-drug composite will not be formed. According to the process of the present invention, the micelle is not produced by merely agitating the block copolymer and the drug, or by just dissolving them in DMF and distilling off the solvent.

As shown in the cited references, some methods for producing micelles were known. However, the process for manufacturing a micelle composed of two components, one of the components being capsulated therein, by dissolving both of the components in a mixed solvent wherein water and an organic solvent form one phase, and distilling off the organic solvent, is not disclosed or suggested by the cited references. Nowhere is it disclosed or suggested that a micelle which is present in an inherently unstable state could be actually formed by such a process.

According to the process for manufacturing a micelle disclosed as the working example in Yokoyama, a micelle is formed by dissolving a block copolymer and drug in DMF alone or in a

mixed solvent of DMF and water and conducting dialysis and ultrafiltration. Although Yokoyama lists but does exemplify other solvents, from the working example using DMF one skilled in the art would have no reasonable expectation whether micelle formation is actually possible by using those solvents of which the physical properties differ from that of DMF. The process for manufacturing a micelle of the present invention, by dissolving a block copolymer and a drug in a mixed solvent of water and a low-boiling point organic solvent miscible with water, distilling off the low-boiling point organic solvent, thereby preparing the micelle formed by the block copolymer and the drug encapsulated therein, is not disclosed or suggested by Yokoyama.

Matsumara points out problems with dialysis and ultrafiltration, but does not at all indicate any alternative steps which may be used.

Sakurai discloses the preparation of a water soluble high molecular polymerized drug. The drug comprises a water-soluble block copolymer comprising a hydrophilic segment and a hydrophobic segment containing a pharmaceutically active side-chain portion. Both dialysis and ultrafiltration are used in the preparation process. A micelle is produced from the compound wherein a block copolymer and a drug are covalently bonded by dialysis and ultrafiltration. The micelle disclosed in Sakurai does not encapsulate a drug in the inner core thereof. Sakurai differs from JP '294 in this regard, and the problems pointed out in Matsumara will not be encountered in Sakurai.

JP '294 discloses a process for producing a micelle,

comprising the steps of dissolving a block copolymer and a drug in chloroform that is an organic solvent not miscible with water, emulsifying the solution in water, and distilling off the chloroform. The characteristic feature of this process is to form an emulsion in water by using an organic solvent non-miscible with water and subsequently removing the organic solvent. This process uses neither dialysis nor ultrafiltration. However, chlorine-based solvents such as chloroform cannot be industrially used in view of environmental protection issues. Further, the method for producing a micelle after forming an emulsion in water is a well-known technique. In contrast, an emulsion is not formed in the instant process. The process for manufacturing a micelle of the present invention, by dissolving a block copolymer and a drug in a mixed solvent wherein water and an organic solvent form one phase, and distilling off the organic solvent, is not disclosed or suggested. That is to say, the process of the present invention is not obvious in view of the process for manufacturing a micelle disclosed in JP '294, wherein water and an organic solvent are present in two separate phases. Moreover, in view of the difference in solvents used, one skilled in the art would not be motivated to eliminate the dialysis and ultrafiltration processes of Yokoyama and Sakurai in view of JP '294.

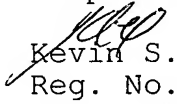
The Examiner provisionally rejects claims 1-8 on the grounds of obviousness-type double patenting as being unpatentable over claims 1-19 of Application Serial No. 10/481,347.

The provisional rejection is respectfully traversed.

Application Serial No. 10/481,347 has issued as U.S. Patent No. 7,138,490. The issued claims relate to a method for manufacturing a block copolymer of polyethylene glycols and poly(acidic amino acid), or a salt thereof, with a content of not more than 10% by weight impurities consisting of polyethylene glycols and poly(amino acidic amino acids), by refining polyethylene glycols by an ion exchange resin, forming a block copolymer of the refined PEG with poly(acidic amino acid), removing a protective group if present, and refining by a partition/adsorption resin. These claims in no way disclose or suggest the process of the claims of the instant application, which require dissolving the AB type block copolymer composed of hydrophilic polymer structure moiety and hydrophobic polyamino acid structure moiety with a drug in a mixed solvent of water and a low-boiling point organic solvent miscible with water.

Reconsideration and allowance are respectfully requested in view of the foregoing.

Respectfully submitted,



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